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August 31, 2005

EUROPEAN PATENT OFFICE
D-80298 Munich
GERMANY
Fax: 49-89-2399-4465
Authorized Officer: Seufert, G.

Re: International Application No. PCT/IB2005/001044
Warner-Lambert Company LLC
Docket No. PC32225APCT

RESPONSE TO WRITTEN OPINION OF THE INTERNATIONAL PRELIMINARY EXAMING AUTHORITY

Dear Sirs,

This communication is being submitted in response to the Written Opinion of the International Searching Authority dated July 12th, 2005. A Demand has been filed for the above referenced application. Thus, this communication is directed to the International Preliminary Examining Authority ("IPEA"). The ISA has rejected claims 1, 2, 7, and 10-12 as lacking novelty. The ISA has acknowledged that claims 3-6, 8, and 9 are novel and possess an Inventive Step.

In order to advance the prosecution of the application, the claims are being amended. Claim 1 has been amended to specify that X^1 is trifluoromethyl or chloro and is located at the 3-position of the phenyl ring. Claim 3 has been cancelled. Claim 7 has been cancelled, to moot the rejection for lack of

industrial utility. Prodrug has been deleted from claim 1 to over the objection to clarity.

Claims 1-12 have been renumbered as claims 1-10 in light of these cancellations. Replacement pages 59-65 are being submitted with this letter showing the amended claims. It is respectfully submitted that claims 1-10 are novel and possess an inventive step. A positive International Preliminary Examining Report is hereby requested.

8/31/05

Date

Respectfully submitted,

J. Michael Dixon
Attorney for Applicant(s)
Reg. No. 32,410

Warner-Lambert Company
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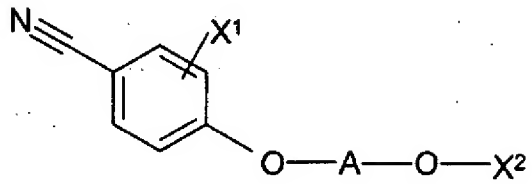
CLAIMS

What is claimed is:

1. A compound of the formula:



a salt or a solvate, thereof,

in which;

a) X^1 is represented by trifluoromethyl or chloro, and is located at the 3-position of the phenyl ring,

b) A is represented by a linear alkylene group containing from 2 to 10 carbon atoms, in which up to 6 hydrogen atoms may optionally be replaced by a substituent independently selected from the group consisting of:

i. halogen,
ii. cyano,
iii. hydroxy,
iv. $(C_1\text{-}C_{12})$alkyl, optionally substituted,
v. $(C_2\text{-}C_{12})$alkenyl, optionally substituted,
vi. $(C_2\text{-}C_{12})$alkynyl, optionally substituted,
vii. $(C_3\text{-}C_{10})$cycloalkyl, optionally substituted,
viii. $(C_3\text{-}C_{10})$ cycloalkyl$(C_1\text{-}C_6)$alkyl, in which the alkyl and cycloalkyl moieties may each be optionally substituted,
ix. $(CH_2)_n\text{-}SR^1$,
x. $(CH_2)_n\text{-}O\text{–}R^1$,
xi. $(CH_2)_n\text{-}NR^1R^2$,
xii. $(CH_2)_n\text{-}COOR^3$ and,

xiii. $(CH_2)_n$-$CONR^4$;

c) X^2 is represented by $(C_6$-$C_{10})$aryl, optionally substituted;

d) n, at each occurrence, is independently represented by an integer from 0 to 6;

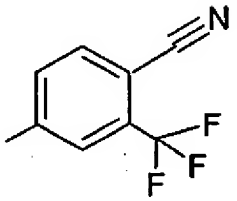
e) R^1 and R^2 are each independently represented by a substituent selected from the group consisting of hydrogen and $(C_1$-$C_6)$alkyl, optionally substituted;

f) R^3 is represented by a substituent selected from the group consisting of hydrogen, and $(C_1$-$C_6)$alky, optionally substituted, and;

g) R^4 is represented by a substituent selected from the group consisting of hydrogen, and $(C_1$-$C_6)$alkyl, optionally substituted.

2. A compound according to claim 1 in which A is represented by ethylene, propylene, butylenes, or pentylene, any of which may be optionally substituted.

3 A compound according to claim 1 or 2 in which X^2 is represented by:



4. A compound according to claim 1, 2, or 3 in which A is ethylene or propylene and is substituted with at least one substituent represented by $(CH_2)_n$-O–R^1 or $(C_1$-$C_6)$alkyl.

5. A compound according to claim 1 selected from the group consisting of:

a. 4,4'-[(2S,3S)-butane-2,3-diylbis(oxy)]bis[2-(trifluoromethyl)benzonitrile]);

b. 4,4'-[(2R,3R)-butane-2,3-diylbis(oxy)]bis[2-(trifluoromethyl)benzonitrile];

c. 4,4'-[but-1-ene-3,4-diylbis(oxy)]bis[2-(trifluoromethyl)benzonitrile];

d. 4,4'-[pentane-1,2-diylbis(oxy)]bis[2-(trifluoromethyl)benzonitrile];

e. 4,4'-[(3-methoxypropane-1,2-diyl)bis(oxy)]bis[2-(trifluoromethyl)benzonitrile];

f. 4,4'-[(3-ethoxypropane-1,2-diyl)bis(oxy)]bis[2-(trifluoromethyl)benzonitrile];

g. 4,4'-[[3-(isopropylamino)propane-1,2-diyl]bis[2-(trifluoromethyl)benzonitrile];

h. 4,4'-[(6-methylhexane-1,2-diyl)bis(oxy)]bis[2-(trifluoromethyl)benzonitrile];

i. 4,4'-[octane-1,2-diylbis(oxy)]bis[2-(trifluoromethyl)benzonitrile];

j. 4-[1-(4-Cyano-3-trifluoromethyl-phenoxymethyl)-2,2-dimethyl-cyclopropoxy]-2-trifluoromethyl-benzonitrile;

k. 4,4'-[Propane-1,3-diylbis(oxy)]bis[2-(trifluoromethyl)benzonitrile];

l. 4,4'-[(2-methylpropane-1,3-diyl)bis(oxy)]bis[2-(trifluoromethyl)benzonitrile];

m. 4,4'-[butane-1,3-diylbis(oxy)]bis[2-(trifluoromethyl)benzonitrile];

n. 4-({(3R)-3-[4-cyano-3-(trifluoromethyl)phenoxy]butyl}oxy)-2-(trifluoromethyl)benzonitrile;

o. 4-({(3S)-3-[4-cyano-3-(trifluoromethyl)phenoxy]butyl}oxy)-2-(trifluoromethyl)benzonitrile;

p. 4-{3-[4-cyano-3-(trifluoromethyl)phenoxy]-1,2-dimethylpropoxy}-2-(trifluoromethyl)benzonitrile;

q. 4,4'-[hex-1-ene-4,6-diylbis(oxy)]bis[2-(trifluoromethyl)benzonitrile];

r. 4,4'-[(3-methylbutane-1,3-diyl)bis(oxy)]bis[2-(trifluoromethyl)benzonitrile];

s. 4-{[3-(4-cyanophenoxy)-2-ethylhexyl]oxy}bis[2-(trifluoromethyl)benzonitrile];

t. 4,4'-[(2S,4S)-pentane-2,4-diylbis(oxy)]bis[2-(trifluoromethyl)benzonitrile];

u. 4,4'-[heptane-1,4-diylbis(oxy)]bis[2-(trifluoromethyl)benzonitrile];

v. 4,4'-[hexane-2,5-diylbis(oxy)]bis[2-(trifluoromethyl)benzonitrile];

w. 4,4'-[(2S,5S)-hexane-2,5-diylbis(oxy)]bis[2-(trifluoromethyl)benzonitrile];

x. 4-({5-[4-cyano-2-(trifluoromethyl)phenoxy]pentyl}oxy)-2(trifluoromethyl)benzonitrile;

y. 4,4'-[hexane-1,5-diylbis(oxy)]bis[2-(trifluoromethyl)benzonitrile];

z. 4,4'-[(3-methylpentane-1,5-diyl)bis(oxy)]bis[2-(trifluoromethyl)benzonitrile];

aa. 4-(1-methoxymethyl-2-phenoxy-ethoxy)-2-trifluoromethyl-benzonitrile;

bb. 4-(1-hydroxymethyl-2-phenoxy-ethoxy)-2-trifluoromethyl-benzonitrile;

cc. (1R)-4-(1-hydroxymethyl-2-phenoxy-ethoxy)-2-trifluoromethyl-benzonitrile;

dd. (1R)-4-(1-methoxymethyl-2-phenoxy-ethoxy)-2-trifluoromethyl-benzonitrile;

ee. (1S)-4-(1-methoxymethyl-2-phenoxy-ethoxy)-2-trifluoromethyl-benzonitrile;

ff. 2-chloro-4-(2-methoxy-1-phenoxymethyl-ethoxy)-benzonitrile;

gg. 2-chloro-4-(1-phenoxymethyl-butoxy)-benzonitrile;

hh. 2-chloro-4-(1-phenoxymethyl-propoxy)-benzonitrile;

ii. 2-chloro-4-(1-phenoxymethyl-butoxy)-benzonitrile;

jj. 2-chloro-4-[1-(4-methoxy-phenoxymethyl-propoxy)-benzonitrile;

kk. 2-chloro-4-[1-(2-methoxy-phenoxymethyl-propoxy)-benzonitrile;

ll. 2-chloro-4-[1-methyl-phenoxy-ethoxy)-benzonitrile;

mm. 4-[4-(4-cyano-3-trifluoromethyl-phenoxy)- 2-hydroxy-butyloxy]-2-trifluoromethyl-benzonitrile;

nn. 4-[3-(4-cyano-3-trifluoromethyl-phenoxy)- 2-cyclohexyl-propyloxy]-2-trifluoromethyl-benzonitrile;

oo. 4-[3-(4-cyano-3-trifluoromethyl-phenoxy)- 2-cyclohexyl-propyloxy]-2-trifluoromethyl-benzonitrile;

pp. 4-[3-(4-cyano-3-trifluoromethyl-phenoxy)- 2-chloro-propyloxy]-2-trifluoromethyl-benzonitrile;

qq. 4-[8-(4-cyano-3-trifluoromethyl-phenoxy)- 2-chloro-4-hydroxy-octyloxy]-2-trifluoromethyl-benzonitrile;

rr. 4-[10-(4-cyano-3-trifluoromethyl-phenoxy)- 2-methylcyclopentyl-octyloxy]-2-trifluoromethyl-benzonitrile;

ss. 4-[10-(4-cyano-3-trifluoromethyl-phenoxy)- decyloxy]-2-trifluoromethyl-benzonitrile;

tt. 4-[7-(4-cyano-3-trifluoromethyl-phenoxy)-2-cyano-4-methyl-6-hydroxy-heptyloxy]-2-trifluoromethyl-benzonitrile;

uu. 4-(3-(3-hydroxy-4-fluoro-phenoxy)-propoxy)-2-trifluoromethyl-benzonitrile;

vv. 4-(2-cyano-4-dimethylamino-8-phenoxy-octyloxy)-2-trifluoromethyl-benzonitrile;

ww. 4-(2-dimethylamino-2-(4-cyano-phenoxy)-ethyloxy)-2-trifluoromethyl-benzonitrile;

xx. 4-(1-cyclopentyloxymethyl-3-(4-hydroxy-phenoxy)-propoxy)-2-trifluoromethyl-benzonitrile; and

yy. 4-(2-methyl-4-dimethylamino-8-phenoxy-octyloxy)-2-trifluoromethyl-benzonitrile.

6. Use of a compound according to any one of claims 1-5 in the manufacture of a medicament for inhibiting activation of the androgen receptor.

7. Use of a compound according to any one of claims 1-5 in the manufacture of a medicament for alleviating a condition selected from the group consisting of hormone dependent cancers, benign hyperplasia of the prostate, acne, hirsutism, excess sebum, alopecia, premenstrual syndrome, lung cancer, precocious puberty, osteoporosis, hypogonadism, age-related decrease in muscle mass, and anemia.

8. A pharmaceutical composition comprising a compound according to any one of claims 1-5 in admixture with one or more pharmaceutically acceptable excipients.

9. A topical pharmaceutical formulation comprising a compound according to any one of claims 1-5 in admixture with or more pharmaceutically acceptable excipients suitable for dermal application.

10. An article of manufacture comprising a compound according to any one of claims 1-5 packaged for retail distribution, which advises a consumer how to utilize the compound to alleviate a condition selected from the group consisting of acne, alopecia, and oily skin.

Confirmation Report – Memory Send

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